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Swiss medical centres vary significantly when it comes to outcomes of neonates with a very low gestational age

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Abstract: AIM This study quantified the impact of perinatal predictors and medical centre on the outcome of very low-gestational-age neonates (VLGANs) born at <32 completed weeks in Switzerland. **METHODS** Using prospectively collected data from a 10-year cohort of VLGANs, we developed logistic regression models for three different time points: delivery, NICU admission and seven days of age. The data predicted survival to discharge without severe neonatal morbidity, such as major brain injury, moderate or severe bronchopulmonary dysplasia, retinopathy of prematurity (stage three) or necrotising enterocolitis (stage three). **RESULTS** From 2002 to 2011, 6892 VLGANs were identified: 5854 (85%) of the live-born infants survived and 84% of the survivors did not have severe neonatal complications. Predictors for adverse outcome at delivery and on NICU admission were low gestational age, low birthweight, male sex, multiple birth, birth defects and lack of antenatal corticosteroids. Proven sepsis was an additional risk factor on day seven of life. The medical centre remained a statistically significant factor at all three time points after adjusting for perinatal predictors. **CONCLUSION** After adjusting for perinatal factors, the survival of Swiss VLGANs without severe neonatal morbidity was strongly influenced by the medical centre that treated them.

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Swiss medical centres vary significantly when it comes to outcomes of neonates with a very low gestational age

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ABSTRACT

Aim: This study quantified the impact of perinatal predictors and medical centre on the outcome of very low gestational age neonates (VLGANs) born at less than 32 completed weeks in Switzerland.

Methods: Using prospectively collected data from a 10-year-cohort of VLGANs, we developed logistic regression models for three different time points: delivery, NICU admission and seven-days-of-age. The data predicted survival to discharge without severe neonatal morbidity, such as major brain injury, moderate or severe bronchopulmonary dysplasia, retinopathy of prematurity (\geq stage three) or necrotising enterocolitis (\geq stage three).

Results: From 2002-2011, 6,892 VLGANs were identified: 5,854 (85%) of the live born infants survived and 84% of the survivors did not have severe neonatal complications. Predictors for adverse outcome at delivery and on NICU admission were: low gestational age, birth weight, male sex, multiple birth, birth defects and lack of antenatal corticosteroids. Proven sepsis was an additional risk factor on day seven of life. The medical centre remained a statistically significant factor at all three time points after adjusting for perinatal predictors

Conclusion: After adjusting for perinatal factors, the survival of Swiss VLGANs without severe neonatal morbidity was strongly influenced by the medical centre that treated them.

Key words: neonatal morbidity, outcome variability, perinatal predictors, survival, very low gestational age neonates

Key notes

- This study quantified the impact of perinatal predictors and medical centre on the outcome of very low gestational age neonates (VLGANs).
- Using prospectively collected data, we identified 6,892 VLGANs born in Switzerland at less than 32 weeks of gestation between 2002-2011.
- Important predictors for adverse outcomes were patient-level factors, obstetrical interventions, proven sepsis in the first week of life and the medical centre where the neonate was treated.

ABBREVIATIONS

ANC, antenatal corticosteroids

BPD, bronchopulmonary dysplasia

CI, confidence interval

GA, gestational age

NICU, neonatal intensive care unit

NEC, necrotising enterocolitis

OR, odds ratio

PIVH, periventricular/intraventricular haemorrhage

PVL, periventricular leukomalacia

ROP, retinopathy of prematurity

VLGANs, very low gestational age neonates

INTRODUCTION

Survival rates and survival without morbidity increase sharply with gestational age (GA) among very low GA neonates (VLGANs) born at less than 32 completed weeks and GA has traditionally

been used as the sole outcome predictor. More recently, models that have included perinatally known factors, such as estimated foetal weight, gender, single or multiple birth, antenatal corticosteroid (ANC) administration and delivery mode have been shown to increase the accuracy of predicting survival (1-3).

Variations in the survival rates of preterm neonates have been observed between centres providing healthcare in several populations and networks (4-7). Factors contributing to these differences in outcome have included the inherent risk of the patient population served, the local approach towards primary non-intervention at the border of viability and, or, the effectiveness of the patient care delivered at a particular medical centre. Despite the availability of national guidelines on perinatal care at the limit of viability, between 22 and 26 completed weeks of gestation (8), survival rates vary widely across the nine tertiary level perinatal centres in Switzerland, even after adjusting for important patient-related factors (9,10).

The chance of survival changes rapidly throughout the first week of life in infants born at less than 32 weeks of gestation, due to the fact that mortality is highest during the first few days of life. Therefore, predictors for survival and short-term morbidity may vary depending on postnatal age.

Existing models that aim to predict survival or morbidity rates of VLGANs do not address the potential centre effect on outcome and do not take into account the rapidly changing chances of survival during the first few days of life. Therefore, we sought to quantify the impact of different perinatal predictors and medical centre on survival and short-term morbidity at three different time points in infants born at less than 32 weeks in Switzerland.

MATERIALS AND METHODS

Data sources

The Swiss Neonatal Network and Follow-Up Group maintains a database, the Minimal Neonatal Data Set (MNDS), to prospectively collect anonymised information about the demographics and outcome to the point of hospital discharge of all live born infants weighing between 400 and 1,500g at birth and with a GA of between 23 0/7 and 31 6/7 weeks. It covers infants born at, or transferred, to one of the nine level III Neonatal Intensive Care Units (NICUs) caring for VLGANs in Switzerland. Data collection and evaluation were approved by the institutional ethical review boards and by the Swiss Federal Commission for Privacy Protection in Medical Research. In the present study, data from the Swiss MNDS was used to analyse information on all VLGANs of 23–31 completed weeks born between 1 January 2002 and 31 December 2011.

Definition of neonatal variables

GA was calculated based on ultrasound examinations during the first trimester of pregnancy and defined as the postmenstrual age in weeks and days. Birth weight standard deviation scores (z-scores) for GA were calculated based on the growth curves published by Voigt et al (11).

ANC administration was considered to have occurred if at least one dose was given prenatally.

Major congenital malformation was defined as any type of malformation that had a severe impact on prognosis, such as complex congenital heart disease or malformation syndromes. Neonatal sepsis was assumed if positive blood cultures were present. We defined major brain injury as periventricular/intraventricular haemorrhage (PIVH) \geq grade 3 (12) and, or, cystic periventricular leukomalacia (PVL) (13). Diagnosis of moderate or severe bronchopulmonary dysplasia (BPD) was based on the National Institute of Child Health and Human Development consensus definition

as a requirement for supplemental oxygen and, or, mechanical respiratory support at 36 weeks of postmenstrual age (14). Severe retinopathy of prematurity (ROP) was defined as \geq stage 3 as suggested by the International Committee for the Classification of Retinopathy of Prematurity (15). Necrotising enterocolitis (NEC) was diagnosed in the presence of at least intestinal pneumatosis and, or, portal venous gas (Bell's stage \geq 2) (16).

Outcome definition

The main outcome assessed was survival to discharge without severe neonatal morbidity, in other words without major brain injury, moderate or severe BPD, ROP \geq stage 3 or NEC \geq stage 2.

Time points of risk assessment

Outcome predictors were evaluated at delivery, on NICU admission and on the seventh day of life. Infants who had already died at a previous assessment time point were excluded from the following assessments.

Statistical analysis

Missing data and multiple imputation

Missing data were more frequent in non-survivors than in survivors, raising concerns about overestimating survival and other bias. To prevent case-wise deletion of infants from analyses, we imputed missing predictor values using the multivariate normal model and generated 10 completed data sets, resulting in imputed variables of binary variables taking on non-integer values, which were then carried forward without performing rounding (17, 18). Data was imputed for survivors and non-survivors. All non-missing predictors and outcomes were included in the imputation model.

Predictors

Predefined predictors with high *a priori* plausibility were evaluated. The following prenatal predictors were tested at all time points: GA, z-score for birth weight, gender, singleton/multiple birth, ANC, mode of delivery, major congenital malformation and the medical centre where the infants were cared for. In addition, sepsis within the first seven days of life was evaluated at the seventh day of life.

Model assessment and selection

The following candidate logistic regression models for the binary outcomes of survival to discharge without severe neonatal morbidity were evaluated for each time point:

- A. GA as the only predictor
- B. All considered predictors except medical centre
- C. Applying backward elimination to model B
- D. Model B including medical centre
- E. Applying backward elimination to model D

Backward elimination was performed by dropping non-significant predictors (p value > 0.05) one at a time until all the predictors had a p value of < 0.05 .

The continuous predictors GA and z-score for birth weight were tested for departure from linearity. Non-linearity was addressed by including GA as a categorical variable, by weeks, and birth weight by categorising the z-score. Following the usual convention, z-score for birth weight was split into ten 0.5 range categories from less than -2 to more than +2.

We chose one primary model from A-E for each time point using the following procedure: the cross validated c-statistic was calculated across the 10 multiple imputed datasets. This resulted in 10 c-statistics for each model, which were combined using Rubin's rule to provide the final cross validated c-statistic and confidence interval (CI) for each model (19). For each time point, the model with the highest cross-validated c-statistic was chosen as the final prediction model.

Calibration of the models was assessed with plots.

The models were screened for statistically significant interactions, using the p value of the Wald test for the interaction term < 0.05 . This showed that including any of the interaction terms did not improve the cross-validated c-statistics. However, to examine centre-to-centre difference based on GA groups, we fitted the final models to include an interaction term for GA groups (< 25 weeks, 25-27 weeks or > 27 weeks) and medical centre.

Prediction

We calculated predicted survival probabilities and their 95% CIs from the combined estimates of the multiple imputed datasets by applying Rubin's rule (19). All statistical analyses were performed using Stata 13 (StataCorp. 2013. *Stata Statistical Software: Release 13*. College Station, Texas, USA: StataCorp LP).

RESULTS

Between 1 January 2002 and 31 December 2011, 6,892 infants with a GA of between 23 and 31 completed weeks were cared for at the nine level III perinatal centres in Switzerland and 5,854 (85%) infants survived. Of all the deaths, 394 (38%) occurred in the delivery room and 644 (62%) occurred in the NICU: 405 (63%) of the NICU deaths occurred early, within seven days of

admission, and 239 (37%) occurred after the seventh day of life. Of the 5,854 survivors, 4,905 (84%) survived the neonatal period without any severe neonatal complications. Table 1 summarises the characteristics of the patient population.

The cross-validated c-statistics of the five models for each time point are listed in Table S1. The models were used for predictions after applying backward elimination for prenatal and postnatal predictors, including the medical centre. Figure S1 shows the calibration plots.

Table 2 lists the logistic regression models with the effects of the various predictors on survival without severe neonatal morbidity.

The medical centre where care was provided was statistically a highly significant predictor of outcome after adjustment for prenatal and postnatal predictors. For example, at delivery, an infant born at medical centre nine, which had the highest overall survival rate, had an odds ratio (OR) for survival without severe neonatal morbidity of 4.5 (95% CI 3.4-6.0), compared to reference centre one, which had the lowest overall survival rate. This exceeded the effect of being born at 25 weeks versus 24 weeks (OR 3.2, 95% CI 2.2-4.6) or even being born at 27 weeks versus 25 weeks (OR 3.8, 95% CI 2.9-5.0). This association with the centre where the infants was treated persisted on NICU admission (OR 3.9, 95% CI 3.0-5.3) and on the seventh day of life after an additional adjustment for proven sepsis during the first week of life (OR 3.4, 95 % CI 2.5-4.6).

When we used the model that allowed interactions between GA groups and centres, the OR for survival without severe morbidity at delivery for an infant born < 25 weeks in centre nine compared to centre one was 4.5 (CI 2.5-8.1). The OR for an infant born between 25 and 27 weeks was 5.3

(CI 3.0-9.3) and for an infant born > 28 weeks it was 3.3 (CI 2.2-4.9). The corresponding ORs for an infant on admission to the NICU were 3.4 (CI 1.89-6.5), 4.6 (CI 2.6-7.9) and 3.0 (CI 2.1-4.4), respectively.

GA-specific prediction estimates and CIs for all time points were calculated for singleton infants without severe malformations with *favourable* perinatal predictors, namely z-score for birth weight of +0.5 to 1, female gender, ANC, and, for the model on day of life seven, no sepsis during first week of life and compared to singleton infants without severe malformations and *unfavourable* perinatal predictors, namely z-score for birth weight of -1 to -0.5, male gender, no ANC, and, for the model on the seventh day of life, proven sepsis during first week of life.

Figures 1a-c and the corresponding Tables S2a-c illustrate the above-mentioned predictions for the entire country, using the model without the centre as a predictor, and the centres with the highest and lowest predicted rates of survival without severe neonatal morbidity - centres one and nine - for the three time points. Findings were similar if only survival to discharge was examined (Figures 2a-c, Tables S3a-c).

As GA increased, the impact of perinatal risk factors, as well as medical centre on survival and survival without severe neonatal morbidity, became less pronounced, although differences persisted up to 31 weeks of gestation.

DISCUSSION

Our study quantifies the impact of different prenatal and postnatal risk factors and medical centre on the probability of survival to discharge without any severe neonatal morbidity in a large national cohort of VLGANs in Switzerland.

Our three prediction models illustrate how prognosis changed rapidly throughout the first week of life. At the lowest GAs - 23 and 24 completed weeks – the chances of survival without severe neonatal morbidity increased substantially for those infants who were admitted to a NICU (Figures 1a, b). This is not surprising, since delivery room deaths in borderline viable infants are usually the result of primary non-intervention rather than failed resuscitation. At the limit of viability, such an approach invariably leads to death (20-22). Despite the availability of national guidelines or legal definitions of human viability, considerable centre-to-centre differences in the initiation of life-sustaining therapies at the limit of viability were documented in many countries and are likely to reflect a particular NICU's culture (23).

In the present study, chances for survival without severe neonatal morbidity were substantially reduced for all VLGANs who sustained an episode of sepsis during the first week of life (Table 2, Figure 1c).

Finally, our study quantifies centre-to-centre outcome variability in this vulnerable population in Switzerland (Figures 1a-c and 2a-c, Tables S2a-c and S3a-c). The fact that centre-to-centre differences existed for both survival to discharge without severe neonatal morbidity and survival to discharge suggests that more proactive treatment approaches resulted in higher survival rates without increasing short-term morbidity rates. Over the last decade, several publications have

addressed centre-to-centre differences in multiple populations and networks (4,5,7,24,25). Three factors provide possible explanations for centre differences: first, the inherent risk of the patient population served by a centre; second, the approach of any given centre towards primary non-intervention in infants born at the border of viability and third, the effectiveness of the patient care delivered at a particular centre. In our study, the association between medical centre and survival without severe neonatal morbidity remained substantial after adjusting for important patient-level factors (Table 2). This is consistent with centre-to-centre outcome differences reported by other networks that could not be explained by differences in patient demographics (5), health insurance coverage (4) or hospital case load (26,27). These findings suggest that differences in centre-specific neonatal practices strongly influence outcome (24,27,28).

The magnitude of the centre-to-centre outcome differences in our study is comparable to the one described by Lee et al for Canadian NICUs (4) and by Vohr et al for the National Institutes for Child Health and Development Neonatal Research Network (NICHD NRN) centres (5). Alleman et al confirmed these findings for a more recent cohort of extremely low birth weight infants cared for by the NICHD NRN and found that centre intervention rates were statistically significant, but only when it came to predicting mortality for infants < 25 weeks GA (24). This contrasts with the results of our study, where centre-to-centre outcome variability extended beyond the most immature infants and primary non-interventions in infants born at the border of viability did not entirely explain the observed centre-to-centre differences. A study by Smith et al from the NICHD NRN found similar results to our study. They reported that that centres with a more aggressive approach to care for infants born at 22-24 weeks also had reduced rates of death, death or ROP, death or NEC, death or late-onset sepsis and death or neurodevelopmental impairment for more mature infants born at 25-27 weeks (29).

Limitations

Because data were more frequently missing in non-survivors, case-wise deletion of infants with missing data from the prediction models would have overestimated survival probabilities. We used multiple imputation to reduce bias due to missing data, but our estimate of the associations could still be biased if missing data depended not only on the variables we used to impute missing values, but also on the unknown missing values themselves (30). A 10-fold cross validation was used to internally validate the models and avoid over-fitting, but the models were not externally validated. Furthermore, we cannot exclude the fact that some of the centre-to-centre differences were a chance finding due to multiple comparisons between the nine NICUs. Our study does not provide information on long-term neurodevelopmental impairment. However, severe neonatal morbidities, such as major brain injuries, moderate/severe BPD, proven NEC and severe ROP, are known to correlate with long-term neurodevelopmental outcomes (31,32). Finally, the study design did not allow us to analyse trends over time.

CONCLUSION

There was strong evidence for wide centre-to-centre outcome variability in rates of survival without severe neonatal morbidity among VLGANs in Switzerland over a time period of 10 years that could not be explained by patient-level factors. The observed outcome differences were not restricted to infants born at the limit of viability, but extended to more mature infants and persisted after the first week of life. Identifying and implementing potentially better practices in perinatal care may influence important outcomes.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in relation to the manuscript.

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SUPPORTING INFORMATION

Figure S1 Calibration plots for the final models for predicting survival without severe neonatal morbidity at different time points

Table S1 10-fold cross-validated c-statistics for different time points and models using the multiple imputed data set

Table S2a-c Predictors for survival without any severe neonatal morbidity* at the time of delivery (a), at the time of NICU admission (b) and on the seventh day of life (c) for inborn singleton infants without major birth defects

Table S3a-c Predictors for survival to discharge at the time of delivery (a), at the time of NICU admission (b) and on the seventh day of life (c) for inborn singleton infants without major birth defects

TABLES

Table 1 Characteristics of study population

		Survivors		Non-survivors	
		5,854		1,038	
			<i>missing</i>		<i>missing</i>
			% (n)		% (n)
Predictors					
Gestational age in weeks and days	mean ± SD	29 2/7 ± 14	0 (0)	26 0/7 ± 16	0 (0)
Birth weight in grams	mean ± SD	1,240 ± 370	0 (0)	840 ± 410	1 (10)
Female	% (n)	46 (2,707)	0 (0)	45 (464)	0.1 (1)
ANC	% (n)	82 (4,823)	4 (234)	52 (537)	13 (138)
Caesarean section	% (n)	78 (4,595)	0.14 (8)	54 (565)	6 (62)
Major congenital malformation	% (n)	3 (201)	0 (0)	16 (164)	0 (0)
Multiples	% (n)	34 (1,966)	0 (0)	25 (263)	0 (0)
Inborn	% (n)	94 (5,479)	0 (0)	95 (982)	1 (12)
Sepsis within first seven days of life [†]	% (n)	3 (166)	2 (117)	6 (58)	23 (236)
Any missing predictor	% (n)		6 (353)		29 (300)
Outcomes					
Died in delivery room	% (n)	NA	NA	38 (394)	0 (0)
Died after admission to NICU but before day of life seven	% (n)	NA	NA	39 (405)	0 (0)
Died after day of life seven but before discharge	% (n)	NA	NA	23 (239)	0 (0)
Moderate or severe BPD	% (n)	9 (548)	0.2 (9)	NA	NA
PIVH ≥ III and/or cPVL	% (n)	6 (323)	0.1 (7)	NA	NA
ROP ≥ stage 3	% (n)	1.8 (103)	0 (0)	NA	NA

NEC	% (n)	1.8 (108)	0 (0)	NA	NA
Any severe neonatal morbidity [§]	% (n)	16 (949)	0.3 (16)	NA	NA

[¶] For infants alive on day of life seven (n=5,705)

[§] Any severe neonatal morbidity: moderate/severe BPD and/or PIVH \geq grade III and/or cPVL and/or proven NEC and or ROP \geq stage III

Abbreviations: ANC: antenatal corticosteroids; BPD: bronchopulmonary dysplasia; cPVL: cystic periventricular leukomalacia; NEC: necrotising enterocolitis; NICU: neonatal intensive care unit; PIVH: periventricular/intraventricular haemorrhage; ROP: retinopathy of prematurity

Table 2 Logistic models of the multiple imputed data for different time points

Outcome	Survival without severe neonatal morbidity*		
Time point	At delivery	On NICU admission	On day of life seven
	OR (95 %CI)	OR (95 %CI)	OR (95 %CI)
Gestational age			
23 weeks	Reference	Reference	Reference
24 vs 23 weeks	13.7 (3.3-57.4)	2.2 (0.61-8.0)	2.6 (0.64-10.3)
25 vs 24 weeks	3.2 (2.2-4.6)	2.3 (1.54-3.3)	1.93 (1.27-2.9)
26 vs 25 weeks	2.3 (1.71-2.97)	2.2 (1.71-3.0)	2.0 (1.48-2.7)
27 vs 26 weeks	1.69 (1.32-2.2)	1.65 (1.30-2.1)	1.55 (1.19-2.0)
28 vs 27 weeks	1.74 (1.36-2.2)	1.70 (1.34-2.2)	1.61 (1.25-2.1)
29 vs 28 weeks	1.29 (1.01-1.66)	1.31 (1.03-1.67)	1.24 (0.96-1.60)
30 vs 29 weeks	1.67 (1.3-2.14)	1.63 (1.28-2.1)	1.66 (1.28-2.16)
31 vs 30 weeks	1.79 (1.37-2.3)	1.68 (1.30-2.2)	1.67 (1.26-2.2)
BW (z-score)			
< - 2	0.16 (0.10-0.24)	0.17 (0.11-0.25)	0.22 (0.14-0.35)
-2 to -1.5	0.37 (0.27-0.51)	0.39 (0.28-0.53)	0.46 (0.33-0.66)
-1.5 to 1	0.51 (0.39-0.65)	0.52 (0.40-0.67)	0.57 (0.43-0.76)
-1 to -0.5	0.69 (0.55-0.86)	0.70 (0.56-0.86)	0.76 (0.60-0.96)
-0.5 to 0	0.94 (0.77-1.15)	0.94 (0.77-1.14)	0.92 (0.74-1.15)
0 to 0.5	Reference	Reference	Reference
0.5 to 1	1.11 (0.88-1.39)	1.08 (0.86-1.34)	1.04 (0.82-1.33)
1 to 1.5	1.27 (0.91-1.77)	1.29 (0.94-1.77)	1.34 (0.93-1.93)
1.5 to 2	0.84 (0.50-1.41)	0.96 (0.57-1.61)	1.06 (0.57-1.96)
> 2	0.14 (0.07-2.63)	0.22 (0.11-0.45)	0.69 (0.22-2.2)
Prenatal steroids	1.60 (1.32-1.94)	1.4 (1.17-1.70)	-
Female	1.39 (1.21-1.59)	1.44 (1.26-1.65)	1.47 (1.27-1.69)
Caesarean section	-	-	-
Multiples	1.17 (1.01-1.36)	1.22 (1.06-1.41)	1.27 (1.08-1.49)
Birth defect	0.19 (0.15-0.25)	0.24 (0.18-0.31)	0.43 (0.31-0.60)
Sepsis first seven days of life	NA	NA	0.49 (0.35-0.70)

Centre

	Reference	Reference	Reference
1			
2	1.68 (1.32-2.1)	1.54 (1.22-1.93)	1.34 (1.05-1.72)
3	2.0 (1.50-2.7)	1.89 (1.42-2.51)	1.66 (1.21-2.3)
4	1.26 (0.87-1.83)	1.14 (0.80-1.63)	1.02 (0.71-1.51)
5	1.67 (1.33-2.1)	1.38 (1.11-1.71)	1.17 (0.92-1.48)
6	2.1 (1.55-2.8)	1.89 (1.43-2.5)	1.45 (1.08-1.94)
7	2.1 (1.68-2.55)	1.89 (1.53-2.3)	1.48 (1.12-1.86)
8	2.8 (2.1-3.6)	2.6 (2.0-3.5)	2.1 (1.58-2.9)
9	4.5 (3.4-6.0)	3.9 (3.0-5.3)	3.4 (2.5-4.6)

* Severe neonatal morbidity: moderate/severe BPD and/or PIVH \geq grade III/IV intracranial haemorrhage and/or cPVL and/or proven NEC and/or ROP \geq stage III

Abbreviations: ANC: antenatal corticosteroids; BPD: bronchopulmonary dysplasia; cPVL: cystic periventricular leukomalacia; NEC: necrotising enterocolitis; NICU: neonatal intensive care unit; PIVH: periventricular/intraventricular haemorrhage; ROP: retinopathy of prematurity

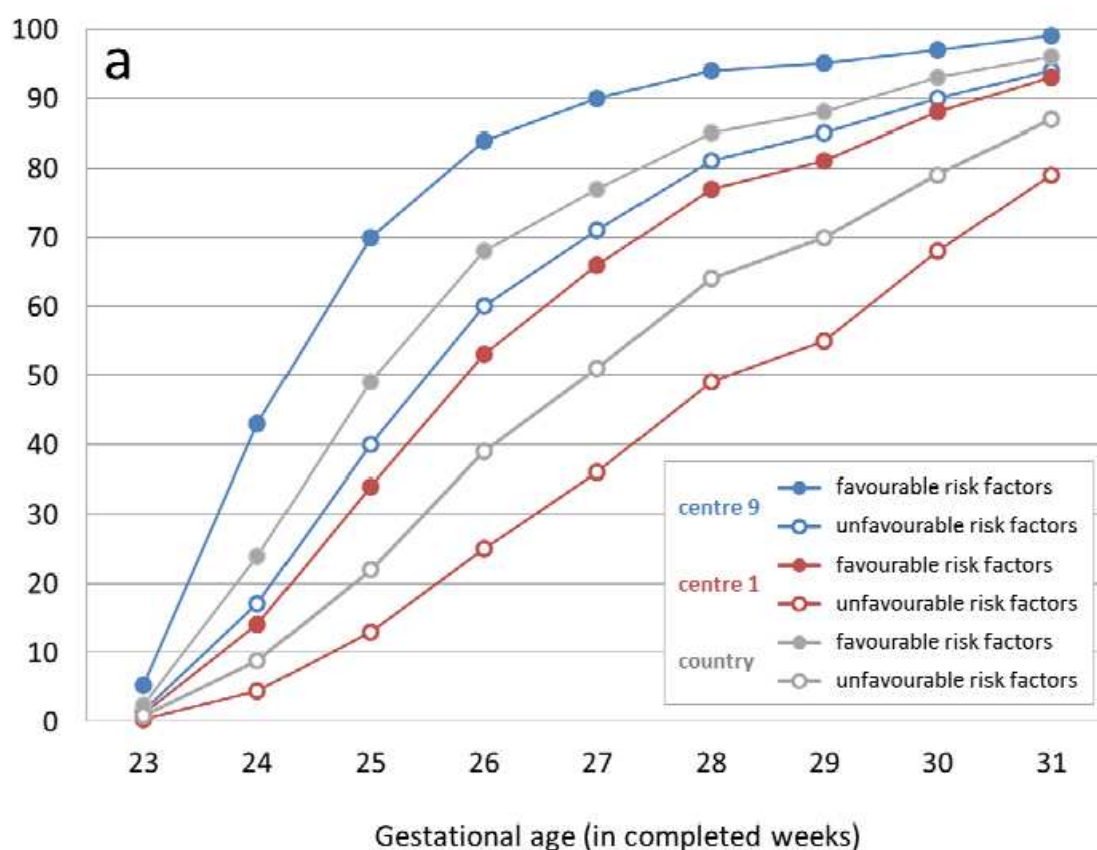
FIGURE LEGENDS

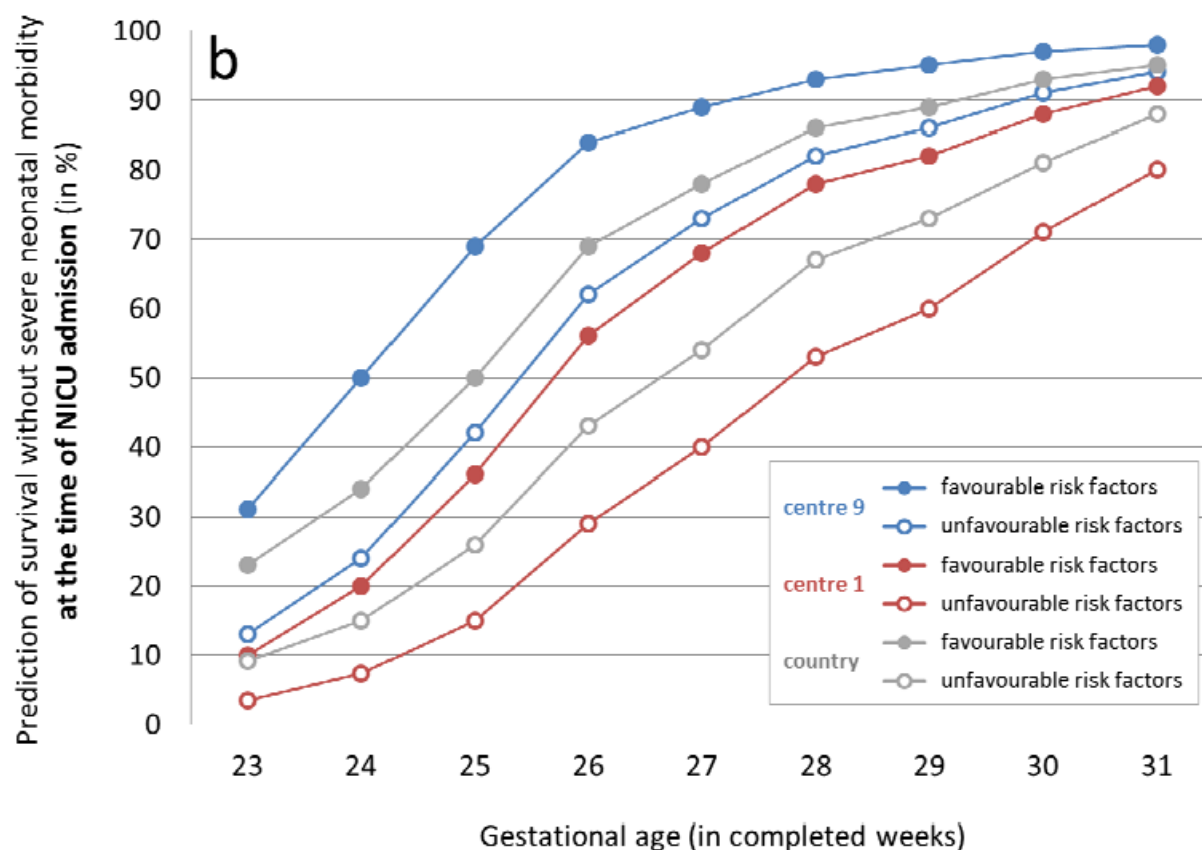
Figure 1 Prediction of survival without severe neonatal morbidity at the time of birth (a), at the time of NICU admission (b) and on day of life seven (c) (favourable risk factors: z-score for BW + 0.5 to 1, female, ANC, and, for the model on day of life seven, no proven sepsis during first week of life; unfavourable risk factors: z-score for BW - 0.5 to -1, male, no ANC, and, for the model on day of life seven, proven sepsis during first week of life).

Figure 2 Prediction of survival to discharge at the time of birth (a), at the time of NICU admission (b) and on day of life seven (c) (favourable risk factors: z-score for BW + 0.5 to 1, female, ANC, and, for the model on day of life seven, no proven sepsis during first week of life; unfavourable risk factors: z-score for BW - 0.5 to -1, male, no ANC, and, for the model on day of life seven, proven sepsis during first week of life).

Figure S1 Calibration plots for the final models for predicting survival without severe neonatal morbidity at different time points.

Prediction of survival without severe neonatal morbidity
at the time of birth (in %)





Prediction of survival without severe neonatal morbidity
on day of life 7 (in %)

